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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/591,787	07/30/2007	Kazuhiro Nagaike	59150-8037	3253

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EXAMINER	
CHEN, STACY BROWN	
ART UNIT	PAPER NUMBER
1648	
MAIL DATE	DELIVERY MODE
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Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	10/591,787	NAGAIKE ET AL.	
	Examiner	Art Unit	
	Stacy B. Chen	1648	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE *3* MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *03 March 2009 and 23 August 2010*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-91* is/are pending in the application.

4a) Of the above claim(s) *5,6,19-40,44-62 and 66-91* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-4,7-18,41-43 and 63-65* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☒ The drawing(s) filed on *05 September 2006* is/are: a)☒ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☒ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☒ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☒ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date *12/12/06; 3/6/07*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

1. Applicant's election without traverse of Group I in the reply filed on March 3, 2009 is acknowledged. The Office notes that the examiner mistakenly typed claims "1-18, 41-43 and 53-65" [emphasis added] in Group I, however, the claims should have been "1-18, 41-43 and 63-65". Any confusion is regretted. In view of the elected species, the region of the ORF of gene 13", claims 5 and 6 are withdrawn from consideration, along with claims 19-40, 44-62 and 66-91, being drawn to non-elected embodiments. Claims 1-4, 7-18, 41-43 and 63-65 are under examination.

Priority

2. Receipt is acknowledged of papers submitted under 35 U.S.C. 119(a)-(d), which papers have been placed of record in the file. Given that there does not appear to be an English translation of the foreign application, 2004-063277, Applicant cannot rely upon the foreign priority papers to overcome any intervening art rejections because a translation of said papers does not appear to have been made of record in accordance with 37 CFR 1.55. See MPEP § 201.15.

Claims Summary

3. The claims are drawn to a recombinant varicella-zoster virus (VZV), also known as human herpes virus type 3, HHV-3. Also claimed are pharmaceutical compositions and vaccines containing the recombinant VZV. The recombinant VZV comprises a bacterial artificial chromosome (BAC) vector sequence that is inserted into a non-essential region of a VZV genome. The insertion is in the ORF of gene 13, a non-essential gene. A non-essential gene is a gene that is not required for the growth of VZV, whereas an essential gene is required.

The BAC vector sequence comprises a recombinant protein dependent recombinant sequences (see definition for some guidance on interpreting this term, pages 46-47, also discussed below in the rejection under 35 U.S.C., 112, second paragraph). The BAC vector comprises a selectable marker (e.g., drug selectable marker, or GFP). In one embodiment, the BAC vector comprises SEQ ID NO: 7.

The VZV genome is derived from a wild type strain (e.g., Oka strain), or a mutant type strain. The genome has mutations in gene 62 (e.g., substitution at position 2210 to G, 3100 to G, 3818 to C, 4006 to G) and gene 6 (e.g., substitution at position 5745 to G). In another embodiment, the B

Also claimed is a recombinant VZV, pharmaceutical composition and vaccine thereof, comprising an essential gene, other than gene 62, and a BAC vector sequence (see claim 41 with dependency back to claim 19). The Office interprets "other than gene 62" as encompassing embodiments that include gene 62 in addition to another essential gene, but not excluding gene 62. Note that claims 41-43 and 63-65 are deemed redundant by the Office since these product claims are identical in content. The process by which the products are made is not expected to alter the structure of the final product.

Claim Rejections - 35 USC § 112

4. The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claims 3, 4, 7 and 11-13 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claim 3 and dependent claims recite, "wherein at least part of the BAC vector genome sequence is inserted into a non-essential region". An insertion occurs at one position in a sequence, thus it is unclear how a part of the sequence can be inserted while the other part is not. If two sites are involved, then there is more than one insertion. Clarification is required.

Claim 7 recites, "wherein the BAC vector sequence comprises recombinant protein dependent recombinant sequence". (Note that there should be an "a" before "recombinant protein".) The specification discloses that "recombinant" in this context means two different homologous nucleic acid molecules encounter each other, crossover occurs, and a new combination of nucleic acid is generated (see page 46). Pages 46-47 disclose the following:

> The term "recombinant protein-independent recombinant sequence" refers to a sequence which causes recombinant protein-independent recombination. The recombinant protein-dependent recombinant sequence causes recombination in the presence of a recombinant protein, but not in the absence of a recombinant protein. A recombinant protein preferably acts specifically on a recombinant protein-dependent recombinant sequence, and does not act on sequences other than the recombinant protein-dependent recombinant sequence.
>
> Examples of representative pairs of a recombinant protein-dependent recombinant sequence and a recombinant protein include, but are not limited to: a combination of a bacteriophage p1-derived loxP (locus of crossover of P1) sequence and a Cre (cyclization recombination) protein, a combination of Flp protein and FRT site, a combination of φC31 and attB or attP (Thorpe, Helena M.; Wilson, Stuart E.; Smith, Margaret C.M., Control of directionality in the site-specific recombination system of the Streptomyces phage φC31., Molecular Microbiology (2000), 38(2), 232-241.), a combination of resolvase and res site (Sadowski P., Site-specific recombinases: changing partners and doing the twist, J. Bacteriol., February 1986; 165(2) 341-7) (generally, Sauer B., Site-specific recombination: developments and applications., Curr. Opin. Biotechnol., 1994 Oct; 5(5): 521-7).

Aside from the specific examples that Applicant has provided, it remains unclear what these recombinant protein dependent recombinant sequences are. Clarification is required.

Claims 11-13 recite, "wherein the varicella-zoster virus genome is derived from" a wild type strain, a mutant strain or Oka strain. These limitations are unclear because the term "derived from" does not set forth the structural contents of the derived genome. In other words, it is not clear what is retained from the original strain in the derived genome. Without further guidance, the metes and bounds of the term cannot be determined.

Claim Rejections - 35 USC § 102

5. The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

Claims 1-4, 8-12, 17, 18, 41-43 and 63-65 are rejected under 35 U.S.C. 102(b) as being anticipated by Horsburgh *et al.* (US Patent 6,277,621 B1, "Horsburgh"). The claims are summarized above. Horsburgh discloses a vector and encoded virus comprising a recombinant VZV containing a BAC vector sequence (see col. 1, lines 50-54, 65-67; col. 3, lines 41-48; and col.10, lines 15-18). The BAC is inserted into a non-essential region of the virus genome, such as UL13 (see col. 6, lines 40-54). Selectable markers, such as drugs and GFP are suggested (see col. 11, lines 18-29; and col. 12, line 67).

Regarding the limitations in claims 11 and 12 concerning the source of the VZV genome, the claim language "derived from" renders the resulting genome unclear as detailed in the

rejection of claims 11 and 12 above under 35 U.S.C., 112, second paragraph. Since there is no particular structure of the genome in claims 11 and 12, any VZV genome is expected to meet the limitations of these claims.

Regarding the virus and compositions of claim 41-43, which contain an essential gene in addition to gene 62, Horsburgh's virus is expected to contain other essential genes because there is no suggestion to delete all essential genes from the genome.

Although Horsburgh does not specifically suggest that the viruses be used as pharmaceutical compositions or vaccines, note that the limitations in claims 17, 18, 42, 43, 64 and 65 do not indicate that there is any additional component to render the actual contents of the composition distinct from a composition comprising the virus. Horsburgh's viruses are expected to be in some sort of culture or medium during their production and storage, which qualifies as a composition. Although the claims call the composition "pharmaceutical compositions" and "vaccines", the only contents of those compositions are the viruses, which is what Horsburgh teaches. Therefore, the claimed subject matter is anticipated by the prior art.

Claim Rejections - 35 USC § 103

6. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

Claims 13, 14 and 15 are rejected under 35 U.S.C. 103(a) as being unpatentable over Horsburgh *et al.* (US Patent 6,277,621 B1, "Horsburgh") in view of WO00/50603 (abstract,

"WIPO abstract). The claims are summarized above. Horsburgh does not disclose mutations in genes 62 and 6 as claimed. However, it appears that these mutations, particularly the mutations of gene 62 are known to be attenuating mutations of a VZV Oka strain. The WIPO abstract discloses particular mutations in gene 62 of VZV Oka strain that render the strain attenuated and useful as a vaccine. With regard to the mutation in gene 6, the WIPO abstract does not speak to this particular mutation. The Office cannot find in the specification where this mutation came from (*i.e.*, Applicant's own work, further elucidation of the attenuated strain of disclosed in the WIPO abstract, *etc.*). Therefore, in the interest of compact prosecution, the Office will presume that the mutation in gene 6 is inherently present in the attenuated Oka strain disclosed in the WIPO abstract. It would have been obvious to have used all of the attenuating mutations of the attenuated Oka strain of the WIPO abstract. One would have been motivated to use all of the mutations in order to ensure its safety as a vaccine.

7. Claims 7 and 16 are rejected under 35 U.S.C. 103(a) as being unpatentable over Horsburgh *et al.* (US Patent 6,277,621 B1, "Horsburgh") in view of Mori *et al.* (US Patent Application Publication 20080226677, filed May 12, 2004, "Mori"). Claim 7 is drawn to an embodiment wherein the BAC vector sequence comprises recombinant protein dependent recombinant sequence. Although the meaning of the claimed subject matter of claim 7 is not clear, Mori discloses the use of such a sequence (see paragraph [0102] on page 8, for example). Claim 16 is drawn to an embodiment wherein the BAC vector sequence comprises SEQ ID NO: 7. Although Horsburgh does not disclose this particular sequence, it would have been obvious to have used any other available BAC vector sequence, such as the sequence taught by Mori as

SEQ ID NO: 401 (100% identical to Applicant's SEQ ID NO: 7). One would have had a reasonable expectation of success because Mori uses human herpesviruses (types 6 and 7) with the BAC vector sequence.

Double Patenting

8. The nonstatutory double patenting rejection is based on a judicially created doctrine grounded in public policy (a policy reflected in the statute) so as to prevent the unjustified or improper timewise extension of the "right to exclude" granted by a patent and to prevent possible harassment by multiple assignees. A nonstatutory obviousness-type double patenting rejection is appropriate where the conflicting claims are not identical, but at least one examined application claim is not patentably distinct from the reference claim(s) because the examined application claim is either anticipated by, or would have been obvious over, the reference claim(s). See, e.g., *In re Berg*, 140 F.3d 1428, 46 USPQ2d 1226 (Fed. Cir. 1998); *In re Goodman*, 11 F.3d 1046, 29 USPQ2d 2010 (Fed. Cir. 1993); *In re Longi*, 759 F.2d 887, 225 USPQ 645 (Fed. Cir. 1985); *In re Van Ornum*, 686 F.2d 937, 214 USPQ 761 (CCPA 1982); *In re Vogel*, 422 F.2d 438, 164 USPQ 619 (CCPA 1970); and *In re Thorington*, 418 F.2d 528, 163 USPQ 644 (CCPA 1969).

A timely filed terminal disclaimer in compliance with 37 CFR 1.321(c) or 1.321(d) may be used to overcome an actual or provisional rejection based on a nonstatutory double patenting ground provided the conflicting application or patent either is shown to be commonly owned with this application, or claims an invention made as a result of activities undertaken within the scope of a joint research agreement.

Effective January 1, 1994, a registered attorney or agent of record may sign a terminal disclaimer. A terminal disclaimer signed by the assignee must fully comply with 37 CFR 3.73(b).

Claims 1-4, 7-18, 41-43 and 63-65 are provisionally rejected on the ground of nonstatutory obviousness-type double patenting as being unpatentable over claims 1, 4, 11-17, 24 and 25 of copending Application No. 12/094,757. Although the conflicting claims are not identical, they are not patentably distinct from each other because the claimed subject matter of the co-pending application falls within the scope of the recombinant BAC instantly claimed.

This is a provisional obviousness-type double patenting rejection because the conflicting claims have not in fact been patented.

Conclusion

9. No claim is allowed.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Stacy B. Chen whose telephone number is 571-272-0896. The examiner can normally be reached on M-F (7:00-4:30). If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Zachariah Lucas can be reached on 571-272-0905. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

/Stacy B Chen/

Primary Examiner, Art Unit 1648